Potential bioterrorism agent: Category A

ARENAVIRAL HEMORRHAGIC FEVERS IN SOUTH AMERICA

DISEASE REPORTING

In Washington

Described in South America, arenaviral infections have never occurred in Washington State. One case without travel to an endemic area may indicate an act of terrorism and constitute a public health emergency.

Purpose of reporting and surveillance

- To identify rare diseases associated with travel.
- To raise the index of suspicion of a possible bioterrorism event if no natural exposure source is identified.

Reporting requirements

- Health care providers: **immediately notifiable to Local Health Jurisdiction**
- Hospitals: **immediately notifiable to Local Health Jurisdiction**
- Laboratories: **immediately notifiable to Local Health Jurisdiction**, specimen submission required
- Local health jurisdictions: **suspected or confirmed cases are immediately notifiable to DOH Communicable Disease Epidemiology: 1-877-539-4344**

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

A severe illness with temperature ≥101^{o}F (38.3^{o}C) of <3 weeks duration, no predisposing factors for hemorrhage, no established alternative diagnosis with at least two of the following:

- Petechial or hemorrhagic rash
- Epistaxis
- Hematemesis
- Hemoptysis
- Hematochezia
- Bleeding from other sites.

Laboratory criteria for diagnosis (to be completed by Level D laboratories only)

- Identification of New World arenaviruses from a clinical specimen.

Case definition

- Probable: a case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a confirmed case, but has appropriate exposure history.
- Confirmed: a case that is laboratory confirmed, or a case that meets the clinical case definition and is not laboratory confirmed, but is epidemiologically linked to a confirmed case.

A. DESCRIPTION

1. Identification

Acute febrile viral illnesses; duration is 7-15 days. Onset is gradual with malaise, headache, retroorbital pain, conjunctival injection and sustained fever and sweats, followed by prostration. There may be petechiae and ecchymoses, accompanied by erythema of the face, neck and upper thorax. An enanthem with petechiae on the soft palate is frequent. Severe infections result in epistaxis, hematemesis, melena, hematuria and gingival hemorrhage; encephalopathies, intention tremors and depressed deep tendon reflexes are frequent. Bradycardia and hypotension with clinical shock are common findings, and leukopenia and thrombocytopenia are characteristic. Moderate albuminuria is present, with many cellular and granular casts and vacuolated epithelial cells in the urine. Case-fatality rates range from 15% to 30% or more.

Diagnosis is made by isolation of virus or detection of antigen in blood or organs; by PCR, or serologically by immunoglobulin M (IgM) capture ELISA; or detection of neutralizing antibody rises or increasing titers by ELISA or IFA. Laboratory studies for virus isolation and neutralizing antibody tests require BSL-4.

2. Infectious Agent

The Tacaribe complex of arenaviruses: Junin for the Argentine disease; the closely related Machupo virus for the Bolivian; Guanarito virus for the Venezuelan; and the Sabia virus for the Brazilian. (These viruses are related to the viruses of Lassa fever and lymphocytic choriomeningitis.)

3. Worldwide Occurrence

Argentine hemorrhagic fever was first described among corn harvesters in Argentina in 1955. About 200-300 cases or more were reported from endemic areas of the Argentine pampas each year prior to widespread immunization; incidence has been around 100

cases or fewer in recent years. Disease occurs primarily from March to October (autumn and winter). It occurs more frequently in males than in females, and mainly in those aged 15 to 60 years.

A similar disease, Bolivian hemorrhagic fever, caused by the related virus, occurs sporadically or in epidemics in small villages of rural northeastern Bolivia. In July-September 1994, there were 9 cases with 7 deaths.

In 1989, an outbreak of severe hemorrhagic illness occurred in the municipality of Guanarito, Venezuela; 104 cases with 26 deaths occurred between May 1990 and March 1991 among rural residents in Guanarito and neighboring areas. Cases have since been reported intermittently, and the virus is still present in rodents.

Sabia virus caused a fatal illness with hemorrhage and jaundice in Brazil in 1990, a laboratory infection in Brazil in 1992 and a laboratory infection treated with ribavirin in the US in 1994.

4. Reservoir

In Argentina, wild rodents of the pampas (primarily *Calomys musculinus*) are the hosts for Junin virus. In Bolivia, *C. callosus* is the reservoir animal. Cane rats (*Zygodontomys brevicauda*) are implicated as the likely reservoir of Guanarito virus. The reservoir of Sabia virus is not known, although a rodent host is presumed.

5. Mode of Transmission

Transmission to humans occurs primarily by inhalation of small particle aerosols derived directly from rodent excreta containing virus, saliva or from rodents disrupted by mechanical harvesters. Virus deposited in the environment may also be infective when secondary aerosols are generated by farming and grain processing, when ingested or by contact with cuts or abrasions. While uncommon, person to person transmission of Machupo virus has been documented in health care and family settings.

6. Incubation period

Usually 7-16 days.

7. Period of communicability

Not often directly transmitted from person to person, although this has occurred in both Argentine and Bolivian diseases.

8. Susceptibility and resistance

All ages appear to be susceptible, but protective immunity of unknown duration follows infection. Subclinical infections occur.

B. METHODS OF CONTROL

1. Preventive measures:

Specific rodent control in houses has been successful in Bolivia. In Argentina, human contact most commonly occurs in the fields, and rodent dispersion makes control more difficult. An effective live attenuated Junin vaccine has been administered to more than 150,000 individuals in Argentina; it is unlicensed in the US. In experimental animals, this vaccine is effective against Machupo but not Guanarito virus.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Strict isolation during the acute febrile period. Respiratory protection may be desirable along with other barrier methods.
c. Concurrent disinfection: Of sputum and respiratory secretions, and blood contaminated materials.
d. Quarantine: None.
e. Immunization of contacts: None.
f. Investigation of contacts and source of infection: Monitoring and, where feasible, control of rodents.
g. Specific treatment: Specific immune plasma given within 8 days of onset is effective in the treatment of Argentine disease. Ribavirin is likely to be useful in all four diseases. See also: Borio L, Inglesby TV, Peters, CJ, et al. Hemorrhagic fever viruses as biological weapons: medical and public health management. JAMA. 2002; 287:2391-2405 (in *Additional Resources*).

3. Epidemic measures

Rodent control; consider immunization.

4. International measures

None.